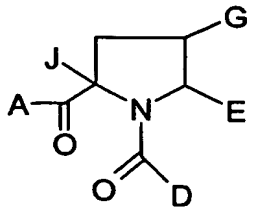
Claims

1. Compounds of Formula (Ia) :



(Ia)

wherein:

A represents hydroxy;

D represents aryl or heteroaryl;

E represents hydrogen, C_{1-6}alkyl, aryl, heteroaryl or heterocyclyl;

G represents hydrogen or C_{1-6}alkyl optionally substituted by one or more substituents selected from halo, OR^1, SR^1, $C(O)NR^2R^3$, CO_2H, $C(O)R^4$, CO_2R^4, NR^2R^3, $NHC(O)R^4$, $NHCO_2R^4$, $NHC(O)NR^5R^6$, $SO_2NR^5R^6$, SO_2R^4, nitro, cyano, aryl, heteroaryl and heterocyclyl;

R^1 represents hydrogen, C_{1-6}alkyl, arylalkyl, or heteroarylalkyl;

R^2 and R^3 are independently selected from hydrogen, C_{1-6}alkyl, aryl and heteroaryl; or R^2 and R^3 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group;

R^4 is selected from the group consisting of C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl; or R^5 and R^6 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group; and

J represents C_{1-6}alkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl;

provided that i) E and G are not both hydrogen; and
ii) the compound is other than
4-ethenyl-1-(2-nitrobenzoyl)-2,2-pyrrolidinedicarboxylic acid, diethyl ester;
1-(2-aminobenzoyl)-4-(1-hydroxyethyl)-2,2-pyrrolidinedicarboxylic acid, diethyl ester;
4-(1-hydroxyethyl)-1-(2-nitrobenzoyl)-2,2-pyrrolidinedicarboxylic acid, diethyl ester;

and salts, solvates and esters thereof; provided that when A is esterified to form -OR

where R is selected from straight or branched chain alkyl, aralkyl, aryloxyalkyl, or aryl, then R is other than *tert*-butyl.

2. A compound as claimed in claim 1 selected from the group consisting of:

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-fluoromethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-hydroxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-hydroxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-allyloxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-propyloxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-isopropenyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-isopropyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

(2S,4S,5R)-2-Isobutyl-1-(3-bromo-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)-pyrrolidine-2-carboxylic acid;

(2S,4S,5R)-2-Isobutyl-1-(3-chloro-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)-pyrrolidine-2-carboxylic acid;

(2S,4S,5R)-2-Isobutyl-1-(3-methyl-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;

rel-(2R,4R,5R)-2-Benzyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(1,3-thiazol-2-yl)-pyrrolidine-2-carboxylic acid;
rel-(2R,4R,5R)-2-Benzyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)-pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(pyrazin-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(pyrazin-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(5-methyl-1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(5-methyl-1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(2-chloro-1,3-thiazol-5-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(2-methoxy-1,3-thiazol-5-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-((methylthio)methyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-((methanesulfonyl)methyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-(1,1-difluoroethyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-(1-hydroxy-1-methylethyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2R,4S,5R)-2-Benzyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(1,3-thiazol-2-yl)-pyrrolidine-2-carboxylic acid;
rel-(2R,4S,5R)-2-Benzyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-2-yl)-pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(pyridin-2-yl)pyrrolidine-2-carboxylic acid;
(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-(1-hydroxy-1-methylethyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-(1-hydroxyethyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(1,3-thiazol-4-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-allyloxymethyl-5-(1,3-

thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-propyloxymethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-cyanomethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-(1-hydroxy-1-methylethyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-tert-butylbenzoyl)-4-ethyl-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(pyrid-2-yl))-pyrrolidine-2-carboxylic acid;
rel(2S,4R,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-(1-methoxyethyl)-5-(1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(pyridin-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-ethoxymethyl-5-(5-methylisoxazol-3-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(5-methoxymethyl-1,3-thiazol-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(5-methylpyridin-2-yl)pyrrolidine-2-carboxylic acid;
rel-(2S,4S,5R)-2-Isobutyl-1-(3-methoxy-4-*tert*-butylbenzoyl)-4-methoxymethyl-5-(thien-2-yl)pyrrolidine-2-carboxylic acid;

and salts, solvates and esters, and individual enantiomers thereof where appropriate.

3. A compound of Formula (Ia) as claimed in claim 1 wherein D represents optionally substituted phenyl.

4. A compound of Formula (Ia) as claimed in claim 3 wherein D represents *para-tert*-butylphenyl optionally further substituted by halo, C_{1-3}alkyl or C_{1-3}alkoxy

5. A compound of Formula (Ia) as claimed in claim 1 wherein E represents optionally substituted heteroaryl.

6. A compound of Formula (Ia) as claimed in claim 5 wherein E represents optionally substituted thiazolyl, pyridinyl, pyrazinyl, isoxazolyl and thienyl.

7. A compound of Formula (Ia) as claimed in claim 1 wherein G represents C_{1-6}alkyl

optionally substituted by halo, OR^1, SR^1, SO_2R^4 and cyano.

8. A compound of Formula (Ia) as claimed in claim 7 wherein G represents C_{1-6}alkyl optionally substituted by OR^1.

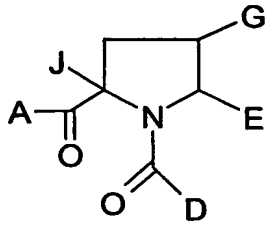
9. A compound of Formula (Ia) as claimed in claim 7 or 8 wherein R^1 represents hydrogen or C_{1-3}alkyl.

10. A compound of Formula (Ia) as claimed in claim 7 wherein R^4 represents C_{1-3}alkyl.

11. A compound of Formula (Ia) as claimed in claim 1 wherein J represents C_{1-6}alkyl, arylalkyl or heteroarylalkyl.

12. A compound of Formula (Ia) as claimed in claim 1, and pharmaceutically acceptable salts and solvates thereof.

13. A method of treating or preventing viral infection which comprises administering to a subject in need thereof, an effective amount of a compound of Formula (I)



(I)

wherein:

A represents hydroxy;

D represents aryl or heteroaryl;

E represents hydrogen, C_{1-6}alkyl, aryl, heteroaryl or heterocyclyl;

G represents hydrogen or C_{1-6}alkyl optionally substituted by one or more substituents selected from halo, OR^1, SR^1, $C(O)NR^2R^3$, CO_2H, $C(O)R^4$, CO_2R^4, NR^2R^3, $NHC(O)R^4$, $NHCO_2R^4$, $NHC(O)NR^5R^6$, $SO_2NR^5R^6$, SO_2R^4, nitro, cyano, aryl, heteroaryl and heterocyclyl;

R^1 represents hydrogen, C_{1-6}alkyl, arylalkyl, or heteroarylalkyl;

R^2 and R^3 are independently selected from hydrogen, C_{1-6}alkyl, aryl and heteroaryl; or R^2 and R^3 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group;

R^4 is selected from the group consisting of C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl; or R^5 and R^6 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group; and

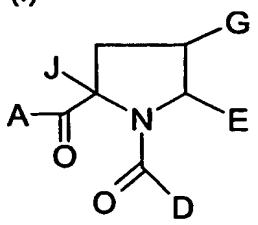
J represents C_{1-6}alkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl;

and salts, solvates and esters thereof; provided that when A is esterified to form -OR where R is selected from straight or branched chain alkyl, aralkyl, aryloxyalkyl, or aryl, then R is other than *tert*-butyl.

14. A method as claimed in claim 13 which involves inhibiting HCV.

15. A method as claimed in claim 13 in which the compound is administered in an oral dosage form.

16. A compound of Formula (I)



(I)

wherein:
A represents hydroxy;

D represents aryl or heteroaryl;

E represents hydrogen, C_{1-6}alkyl, aryl, heteroaryl or heterocyclyl;

G represents hydrogen or C_{1-6}alkyl optionally substituted by one or more substituents selected from halo, OR^1, SR^1, $C(O)NR^2R^3$, CO_2H, $C(O)R^4$, CO_2R^4, NR^2R^3, $NHC(O)R^4$, $NHCO_2R^4$, $NHC(O)NR^5R^6$, $SO_2NR^5R^6$, SO_2R^4, nitro, cyano, aryl, heteroaryl and heterocyclyl;

R^1 represents hydrogen, C_{1-6}alkyl, arylalkyl, or heteroarylalkyl;

R^2 and R^3 are independently selected from hydrogen, C_{1-6}alkyl, aryl and heteroaryl; or R^2 and R^3 together with the nitrogen atom to which they are attached form a 5 or 6

membered saturated cyclic group;

R^4 is selected from the group consisting of C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl; or R^5 and R^6 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group; and

J represents C_{1-6}alkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl;

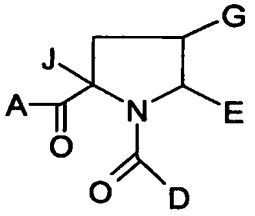
and salts, solvates and esters thereof; provided that when A is esterified to form -OR where R is selected from straight or branched chain alkyl, aralkyl, aryloxyalkyl, or aryl, then R is other than *tert*-butyl;

for use in medical therapy.

17. A compound as claimed in claim 16 wherein the medical therapy is the treatment of viral infection.

18 A compound as claimed in claim 17 wherein the viral infection is HCV.

19 Use of a compound of Formula (I)



(I)

wherein:
A represents hydroxy;

D represents aryl or heteroaryl;

E represents hydrogen, C_{1-6}alkyl, aryl, heteroaryl or heterocyclyl;

G represents hydrogen or C_{1-6}alkyl optionally substituted by one or more substituents selected from halo, OR^1, SR^1, $C(O)NR^2R^3$, CO_2H, $C(O)R^4$, CO_2R^4, NR^2R^3, $NHC(O)R^4$, $NHCO_2R^4$, $NHC(O)NR^5R^6$, $SO_2NR^5R^6$, SO_2R^4, nitro, cyano, aryl, heteroaryl and heterocyclyl;

R^1 represents hydrogen, C_{1-6}alkyl, arylalkyl, or heteroarylalkyl;

R^2 and R^3 are independently selected from hydrogen, C_{1-6}alkyl, aryl and heteroaryl; or R^2 and R^3 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group;

R^4 is selected from the group consisting of C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl;

R^5 and R^6 are independently selected from the group consisting of hydrogen, C_{1-6}alkyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl; or R^5 and R^6 together with the nitrogen atom to which they are attached form a 5 or 6 membered saturated cyclic group; and

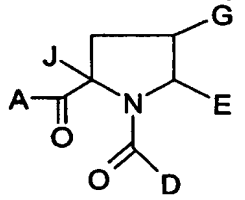
J represents C_{1-6}alkyl, heterocyclylalkyl, arylalkyl or heteroarylalkyl;

and salts, solvates and esters thereof; provided that when A is esterified to form -OR where R is selected from straight or branched chain alkyl, aralkyl, aryloxyalkyl, or aryl, then R is other than *tert*-butyl;
in the manufacture of a medical for the treatment of viral infection.

20 Use as claimed in claim 19, wherein the viral infection is HCV.

21 A pharmaceutical formulation comprising a compound of Formula (Ia) as defined in claim 1 in conjunction with a pharmaceutically acceptable diluent or carrier.

22. A process for the preparation of a compound of Formula (I) as defined in claim 13, comprising treatment of a compound of Formula (II)



(II)

in which A is alkoxy, and D, E, G and J are as defined for Formula (I), with an acid.

23. A process as claimed in claim 22 in which A is *tert*-butoxy.